REMARKS

Claims 35-57 are pending. Claims 37 and 52-57 stand withdrawn from consideration as a non-elected invention under a restriction requirement.

ELECTION/RESTRICTION

Cancellation of the non-elected claims will be reviewed upon notification of allowable subject matter.

SPECIFICATION AND SEQUENCE LISTING

The specification has been amended on page 5 to correct the cross-references in the Figure legends to the Sequence Listing, in accordance with the Examiner's suggestions. On page 20, the specification has been amended to include cross-references to the sequence listing. A revised Sequence Listing will be filed, adding the sequences on page 20, and correcting SEQ ID NO: 4 so that it sets out the sequence of Figure 4.

Rejections Under 35 U.S.C. § 112

All of the claims under consideration stand rejected under 35 U.S.C. § 112, first paragraph, based on the assertion that the specification does not enable one to practice the invention commensurate with the scope of the claims (claims 35, 36, and 38 to 51).

Claim 41 has been cancelled, SEQ ID NO: 4 has been corrected to reflect the sequence of Figure 4 (which has been confirmed to correspond to the cited Genbank reference), and claims 35, 36 and 37 have been amended, as discussed in more detail below.

It is respectfully submitted that the claims as amended are fully enabled by the specification. In this regard, applicants note the examiner's acknowledgement that the specification is enabling for methods of treating hyperlipidemia associated with LPL or ApoE deficiency, comprising the administration of an adenoviral vector containing the coding sequence for an LPL S447X protein. The applicants accordingly request that the Examiner not renew claim rejections under 35 U.S.C. § 112.

DOUBLE PATENTING AND REJECTIONS UNDER 35 U.S.C. § 103

Claims 35, 36, 38, 39, 42-44, 47, 48, and 51 are rejected under the judicially created doctrine of obviousness-type double patenting over Patent No. 6,814,962, and under 35 U.S.C. §103 over WO 96/11276, in view of Kozaki et al as evidenced by Gotada et al.

As set out in Example 2, the LPL S447X therapeutics of the invention have the demonstrable benefit of increasing HDL-C, in addition to significantly decreasing triglyceride levels. This surprising effect is for example set out in the paragraph spanning pages 29 and 30 of the application, as follows (with emphasis added):

> "To demonstrate dose response, LPL +/- mice (n=5/group) were given either $5x10^7$ or $5x10^8$ pfu of either Ad-447 or Ad-LPL (a dose $5x10^7$ pfu is equivalent to approximately $5x10^9$ particles). At a dose of $5x10^8$ pfu of either Ad-LPL or Ad-447 per mouse, there was a significant 2.7 fold increase in plasma LPL activity accompanied by a significant increase in LPL protein levels at day 5 post gene transfer. Corresponding TG, HDL-C and Total-C levels also dropped significantly. At this dose, the only significant difference between the adenovector containing the wild type LPL cDNA versus the Ad-447 was the plasma LPL protein level, which was elevated in the Ad-447 group. Although significantly elevated in both groups over baseline or control mice, post-heparin LPL protein levels were still most profoundly elevated in the Ad-447 group ($p<0.03$). The most provocative differences observed only at the lower dose were in TG and cholesterol measures. **At 3 days post-gene transfer, TG levels were significantly decreased in both Ad-LPL and Ad-447 groups, indicating the efficacy of the transferred LPL in both groups of mice. However, there was a significant increase in both HDL-C and total-C only in the Ad-447 group** ($p<0.01$ and $p<0.03$ respectively, as compared to baseline or Ad-LPL treatment). The magnitude of these alterations, when compared to baseline levels, indicate that the majority of the increase in total-C is within the HDL-C fraction. At this same dose in the Ad-LPL cohort, there was a slight decrease in both total-C and HDL-C with only the decrease in total-C achieving significance ($p=0.04$). This illustrates an increased HDL-C content after adenovirus-mediated gene transfer of the human LPL S447X gene in mice. A similar significant elevation of the HDL-C fraction was observed at day 7, resolving by day 14."

It is respectfully submitted that there is no teaching or suggestion in the cited art that would serve as a basis for a reasonable expectation that LPL S447X therapeutics could be used to treat hyperlipidemia in an amount effective **to lower triglycerides and to raise HDL-C**. Applicants therefore respectfully submit that the present claims distinguish over the cited art.

The previous Action canvases the degree of predictability in the art of the invention. Applicants note in this regard that the cited Kozaki et al. reference clearly indicates that the results reported therein relating to LPL S447X differ from the results reported in the studies of others (Faustinella et al., and Kobayashi et al.), concluding that "further studies are required to know the effect of the Ser447 to stop mutation." Applicants submit that this context reinforces the conclusion that there could have been no *reasonable expectation* that LPL S447X therapeutics *could* be used to treat hyperlipidemia in an amount effective *to lower triglycerides and to raise HDL-C.*

Conclusion

The applicants submit that the claims are in condition for allowance and respectfully request that a timely Notice of Allowance be issued in this case.

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Respectfully submitted,

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